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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,025	05/19/2006	Mitsunori Ono	61251USN(50586)	1888

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Edwards Angell Palmer & Dodge LLP
P.O. Box 55874
Boston, MA 02205

EXAMINER	
YOUNG, SHAWQUIA	
ART UNIT	PAPER NUMBER
1626	
MAIL DATE	DELIVERY MODE
07/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,025	ONO ET AL.	
	Examiner	Art Unit	
	SHAWQUIA YOUNG	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *42-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/16/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-57 are currently pending in the instant application. Claims 1-41 are rejected and claims 42-57 are withdrawn from consideration.

I. *Priority*

The instant application is a 371 of PCT/US04/17064, filed on May 28, 2004 which claims benefit of US Provisional Application 60/474,550, filed on May 29, 2003 and claims benefit of US Provisional Application 60/474,502, filed on May 29, 2003 and claims benefit of US Provisional Application 60/474,410, filed on May 29, 2003.

II. *Information Disclosure Statement*

The information disclosure statement (IDS) submitted on June 16, 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

III. *Restriction/Election*

A. Election: Applicant's Response

Applicants' species election with traverse of compound 12 in the reply filed on March 30, 2009 is acknowledged. The Examiner will group the elected species in a group claims 1-41(in part) drawn to a compound in claim 1 or a composition comprising a compound of formula (I) wherein: Z is N, W is O, S, S(O), S(O2), N or NC(O)RC; X is O, S, S(O), S(O2) or NRC; R1 is N=C(Ra)(Rb); all other variables are as defined in

claim 2. The traversal is on the ground(s) that: (1)consideration and examination of all the exemplary groups suggested by the Examiner should not impose an undue burden.

All of the Applicants' arguments have been considered but have not been found persuasive. It is pointed out that the restriction requirement is made under 35 U.S.C. 121. 35 U.S.C. 121 gives the Commissioner (Director) the authority to restrict applications to several claimed inventions when those inventions are found to be independent and distinct. The Examiner has indicated that more than one independent and distinct invention is claimed in this application and has restricted the claimed subject matter accordingly.

Applicants' argue that consideration and examination of all the exemplary groups suggested by the Examiner should not impose an undue burden. However, the Examiner wants to point out that the various groups are classified in different subclasses in class 514 or 544. Different search considerations are involved (i.e., class/subclass searches, databases searches, etc.) for each of the groups listed. As stated above the inventions are classified into various subclasses in classes 514 and 544. However, each Class 514 and 544 encompasses numerous patents and published applications. For instance, Class 514 contained 165,171 patents and published applications. Therefore it would constitute a burden on the Examiner and the Patent Office's resources to examine the instant application in its entirety. The Examiner also wants to point out that Applicants' instant claims lack unity of invention as discussed in the restriction requirement which allows for the Examiner to impose the restriction requirement. The restriction requirement is deemed proper and made final.

Subject matter not encompassed by elected species which is now grouped into the group claims 1-41(in part) drawn to a compound in claim 1 or a composition comprising a compound of formula (I) wherein: Z is N, W is O, S, S(O), S(O2), N or NC(O)RC; X is O, S, S(O), S(O2) or NRC; R1 is N=C(Ra)(Rb); all other variables are as defined in claim 2 are withdrawn from further consideration pursuant to 37 CFR 1.142 (b), as being drawn to nonelected inventions.

IV. Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising an effective amount of a compound of formula (I) or a pharmaceutically acceptable or prodrug does not reasonably provide enablement for a **solvate** or a **clathrate** of a compound of the formula represented in claim 1. The specification does not provide sufficient guidance nor does it enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), “There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a

disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case

The nature of the invention

The nature of the invention is a compound represented in claim 1 or a composition comprising a compound of formula (I) or a pharmaceutically acceptable salt or prodrug of said compound. There is no teaching of solvates or clathrates of the compounds in claim 1 or a composition comprising a compound of formula(I) in the specification.

The state of the prior art and predictability or lack thereof in the art

It is the state of the prior art that the term "solvate" found in the claims is defined as a compound formed by solvation (the combination of solvent molecules with molecules or ions of the solute. It has been estimated that approximately one-third of the pharmaceutically active substances are capable of forming crystalline hydrates. Predicting the formation of solvates or hydrates of a compound and the number of

molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compound (See *Vippagunta, et al.*)

The scope of "solvate" is not adequately enabled or defined. Applicants provide no guidance as how the compounds are made more active *in vivo*. Solvates and hydrates cannot always be predicted and therefore are not capable of being claimed if the applicant cannot properly enable a particular hydrate or solvate.

The amount of direction or guidance present and the presence or absence of working examples

There is no direction or guidance present in the specification or working examples present in the specification are that defines or relates to what solvates are being included in the elected invention. The term "solvates" is discussed on page 15 of the specification and reads on the following:

"The term solvate is a solvate formed from the association of one or more solvent molecules to one of the compounds of formula (I), formula (I') or formula (I"). The term solvate includes hydrates".

The term "clathrate" is not discussed in any detail in the specification.

The breadth of the claims

The breadth of the claims is a compound represented in claim 1 or a composition comprising a compound of formula (I) or a pharmaceutically acceptable salt, solvate,

clathrate or prodrug of said compound.

The quantity of experimentation needed and the level of the skill in the art

While the level of the skill in the pharmaceutical art is high, the quantity of experimentation needed is undue experimentation. One of skill in the art would need to prepare compounds with various solvents without any direction as to what compounds form solvates or clathrates with which solvents.

The level of skill in the art is high without showing or guidance as to how to make solvates of a compound of formula (I) it would require undue experimentation to figure out the solvents, temperatures and reaction times that would provide solvates or clathrates of the above compounds.

To overcome this rejection, Applicant should submit an amendment deleting the term “solvate” and “clatharate” in the instant claims.

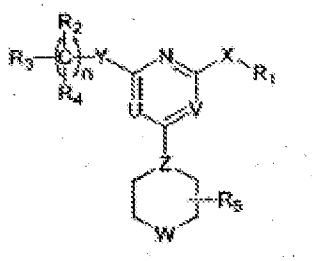
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

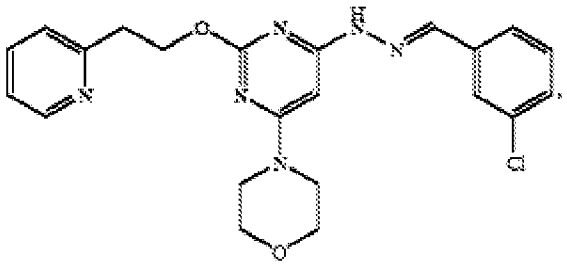
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 2-41 are rejected under 35 U.S.C. 102(e) as being anticipated by *Sun, et al.* (US 6,858,606) or Ono, et al. (US 6,693,097) or Sun, et al. (US 6,660,733). The instant invention claims a composition comprising a product with the formula



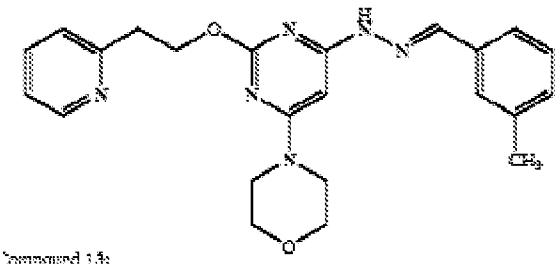
wherein Z is N, W is O, S, S(O), S(O2), N or NC(O)RC; X is O, S, S(O), S(O2) or NRC; R1 is N=C(Ra)(Rb); all other variables are as defined in claim 2.

The *Sun, et al.* reference teaches pyrimidine compounds such as



(See compound 4, column 3) and pharmaceutical compositions comprising these compounds. This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

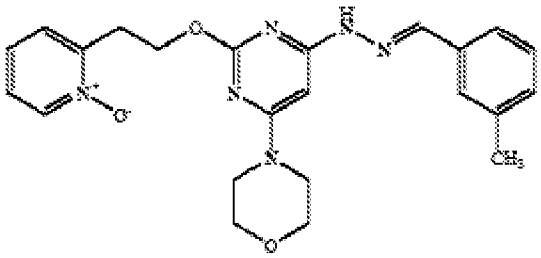
The *Ono, et al.* reference teaches pyrimidine compounds such as



(See compound 12, column 6) and

pharmaceutical compositions comprising these compounds. This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

The *Sun, et al.* reference teaches pyrimidine compounds such as



(See compound 1, column 2) and pharmaceutical compositions comprising these compounds. This species of compound anticipates the genus compound of the instant invention, wherein the genus structure and its definitions are stated above.

35 USC § 103 - OBVIOUSNESS REJECTION

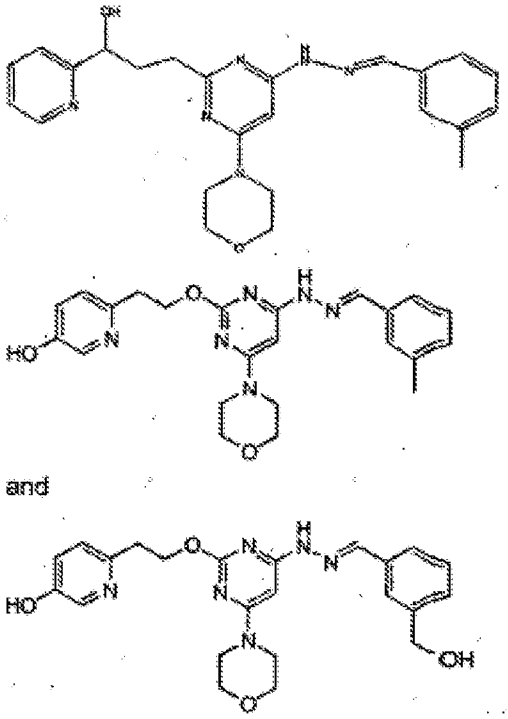
The following is a quotation of 35 U.S.C. § 103(a) that forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Graham v. John Deere Co. set forth the factual inquiries necessary to determine obviousness under 35 U.S.C. §103(a). *See Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Specifically, the analysis must employ the following factual inquiries:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1 is rejected under 35 U.S.C. § 103(a) as being unpatentable over *Ono, et al*. (US Patent 6,693,097). Applicants claim is a compound selected from the group consisting of



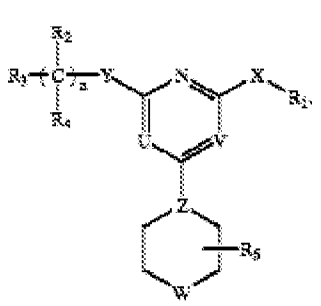
and

.

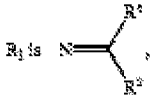
The Scope and Content of the Prior Art (MPEP §2141.01)

Ono, et al. teaches pyrimidine compounds represented by the general formula:

In one aspect, this invention features pyrimidine compounds of formula (I):

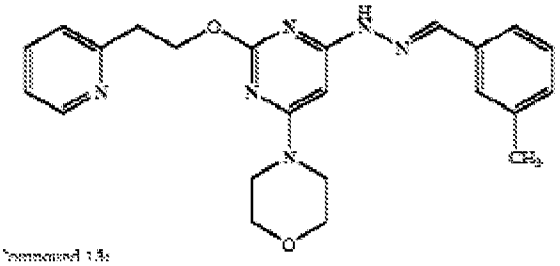


(I)



[referred to hereinafter as $NC(R^aR^b)$], aryl, or heteroaryl; each of R_2 and R_4, independently, is R^c, halogen, nitro, cyano, isothionitro, SR^c, or OR^c; or R_2 and R_4, taken together, is carbonyl; R_3 is R^c, alkenyl, alkynyl, OR^c, $OC(O)R^c$, SO_2R^c, $S(O)R^c$, $S(O_2)NR^cR^d$, SR^c, NR^cR^d, NR^cCOR^d, $NR^cC(O)OR^d$, $NR^cC(O)NR^cR^d$, $NR^cSO_2R^d$, COR^c, $C(O)OR^c$, or $C(O)NR^cR_e$; R_5 is H or alkyl; n is 0, 1, 2, 3, 4, 5, or 6; X is O, S, S(O), $S(O_2)$, or NR^c; Y is a covalent bond, CH_2, C(O), C═N—R^c, C═N—OR^c, C═N—SR^c, O, S, S(O), $S(O_2)$, or NR^c; Z is N or CH; one of U and V is N, and the other is CR^c; and W is O, S, S(O), $S(O_2)$, NR^c, or $NC(O)R^c$; in which each of R^a and R^b, independently, is H, alkyl, aryl, heteroaryl; and each of R^c and R^d, independently, is H, alkyl, aryl, heteroaryl, cyclyl, heterocyclyl, or alkylcarbonyl. Note that the left atom shown in any substituted

The prior art reference also teaches the species



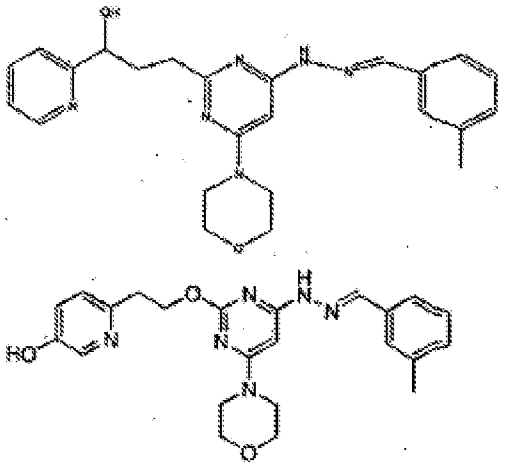
(See compound 12, column 6).

The Difference Between the Prior Art and the Claims (MPEP §2141.02)

The difference between the prior art of *Ono, et al*. and the instant invention is that there is homologous subject matter. For example, the instant compounds have a hydroxy group substituted on the pyridine ring whereas the above species in the prior art does not have a hydroxy group substituted on the pyridine. However, the prior art does teach that the pyridine ring can be substituted with various groups including hydroxy.

Prima Facie Obviousness-The Rational and Motivation (MPEP §2142-2413)

Applicants are claiming a compound selected from the group consisting of



. For example, the prior art reference of *Ono, et al.* teaches a similar compound to the above second compound in the instant application but does not have a hydroxy group attached to the pyridine ring. However, the prior art teaches that the pyridine ring can be optionally substituted with various substituents including hydroxy (See column 3, lines 29-35).

For example, it is obvious to prepare a pyrimidine compound containing a hydroxy-substituted pyridine ring when the art teaches a similar compound wherein the pyridine ring is unsubstituted but can be optionally substituted with various substituents including hydroxy with a reasonable expectation of success. Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to prepare adjacent homologs based on the teachings of the preferred embodiments in the prior art. A strong prima facie obviousness has been established.

Double Patenting

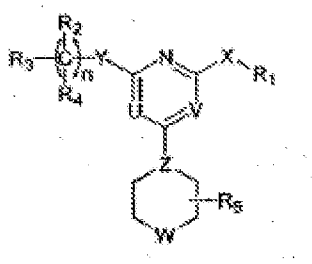
The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-41 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 of U.S. Patent No. 6,858,606 or claims 1-39 of Patent 6,693,097. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Applicants claim a composition comprising a product with the formula

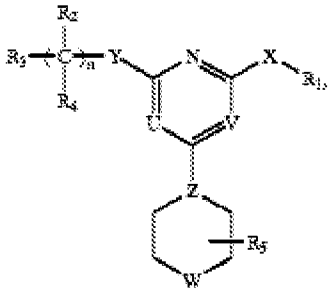


wherein Z is N, W is O, S, S(O), S(O2), N or NC(O)RC; X is O, S, S(O), S(O2) or NRC; R1 is N=C(Ra)(Rb); all other variables are as defined in claim 2.

Determining the Scope and Content of the Issued Patent

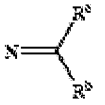
Claim 1 of the issued patent US 6,858,606 is

1. A compound of formula (I):



(I)

wherein R_1 is



in which one of R^a and R^b is H or alkyl, and the other is aryl or heteroaryl optionally substituted with R^d and $R^e{}_m$;

each of R_2 and R_2 is H;

R_3 is H, alkyl, aryl, heteroaryl, cyclyl, heterocyclyl, or alkylcarbonyl;

R_5 is H or alkyl;

n is 0,1, 2, 3, 4, 5, or 6;

X is NR^c;

Y is covalent bond, CH2, C(0), C═N—R^c, C═N—OR^c, C═N—SR^c, 0, S, S(0), S(02), or NR^c;

Z is N or CH;

one of U and V is N, and the other is CR^c and

W is O, S, S(O), S(O2), NR^c, or $NC(0)R^c$;

in which R^c is H, alkyl, aryl, heteroaryl, cyclyl, heterocyclyl, or alkylcarbonyl;

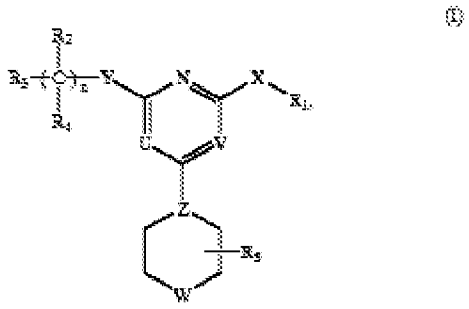
R^d is halogen, CN, alkyl, alkyloxy, alkylcarbonyl, alkyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, hydroxyalkyl, alkylamino, or alkylaminocarbonyl;

Re is halogen, CN, hydroxyl, alkyl, aryl, heteroaryl, alkoxyl, aryloxyl, or heteroaryloxyl; and

m is 0, 1, 2, 3, or 4.

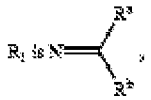
Claim 1 of the issued patent US 6,693,097 is

What is claimed is:
1. A compound of formula (I)



(I)

wherein



aryl, or heteroaryl;
each of R_2 and $R_{2'}$, independently, is R^c, halogen, nitro, cyano, isothiocnitro, SR^c, or OR^c; or R_2 and $R_{2'}$, taken together, is carbonyl
R_3 is R^c, alkenyl, alkynyl, OR^c, $OC(O)R^c$, SO_2R^c, $S(O)R^c$, $S(O_2)NR^cR^d$, SR^c, NR^cR^d, NR^cCOR^d, $NR^cC(O)$

Ascertaining the Differences Between the Instant Application and the Issued Patent

The difference between the instant claims and the issued patent's claims is that the instant claims are drawn to a composition comprising a compound of formula (I) whereas the issued patent's claims are drawn to a compound of formula (I).

Finding Prima Facie Obviousness

The issued patent's claims are drawn to a compound of formula (I) which contains overlapping subject matter with the compound of formula (I) in the claimed composition in the instant application. It has been well established in Ex parte Dourous,

163 USPQ 667 (PTO Bd. App. 1968), that it is obvious to add a carrier to an obvious compound. Therefore, one of ordinary skill in the art would be motivated to prepare a composition comprising the compounds that were claimed in the issued patent since the scope already patented falls within the full scope of the instant claims 2-41. As a result, the claims are rejected under obviousness-type double patenting.

Claims 2-41 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4-33 of US Patent 7,470,685 or 2-38 and 46 of US Patent 7,067,514 or 1-25 of US Patent 6,660,733. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims 2-41 provide products which generically overlap with the issued patent's claimed products and the issued patent provide species in claim 31 in patent 7,470, 685 or claim 46 in patent 7,067,514 or claim 25 in patent 6,660,733 which anticipates the instant application's claimed invention.

This is a non provisional obviousness-type double patenting rejection because the conflicting claims have been patented.

V. Objections

Claim Objection-Non Elected Subject Matter

Claims 2-41 are objected to as containing non-elected subject matter. To overcome this objection, Applicant should submit an amendment deleting the non-elected subject matter.

VI. Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 7:00 AM-3:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shawquia Young/
Examiner, Art Unit 1626
/Rebecca L Anderson/
Primary Examiner, Art Unit 1626